REMARKS

In an Office Action dated February 25, 2004, claims 44-59, all of the claims under consideration in the subject patent application, were rejected. By amendment above, claims 44, 46, 48, 50, 53, 54, 55 and 58 have been rewritten, claim 52 has been cancelled and claims 60-64 have been added. Support for the amendments to claims 44, 46, 48 and 50 can be found on pages 9-10 of the specification, and in the claims as originally filed. Support for the amendments to claims 53 and 54 can be found in claim 52, as claim 52 is now incorporated into these claims. Support for the amendments in claims 55 can be found on page 23 of the specification. Support for the amendments to claim 58 can be found on page 29 lines 6-7 of the specification. Support for new claims 60-64 can be found in claims 55-59.

Reconsideration of this application and allowance of the claims is respectfully requested in view of the foregoing amendments and the following remarks.

The Examiner has objected to the specification for not complying with 37 CFR 1.821(d) of the Sequence Rules and Regulations. According to the Examiner the specification of the patent application discusses a sequence listing however sequences have been disclosed without the used of the assigned identifier (SEQ ID NO:). Applicants submit that the specification has been amended to include the sequence identifier in the text of the specification. Accordingly, applicants submit that the specification complies with 37 CFR 1.821(d) and withdrawal of the rejection is respectfully requested.

The Examiner objected to the amendment filed December 17, 2003 because she asserts that it introduces new matter. According to the Examiner the claim language "wherein the

response is measured in step (c) is selected from GTPγS binding" in claim 55 and "wherein the cytokines are selected from the group consisting of MCP" in claim 58 is not supported by the original disclosure. The Examiner further rejected claims 55 and 58 under 35 USC §112, first paragraph, for failing to comply with the written description requirement because the claims contain subject matter which was not described in the specification in such a way as to reasonably convey that the inventors had possession of the claimed invention. The Examiner asserts that the amendment to claims 55 and 58 filed December 17, 2003, is not supported by Examples 14-19 as pointed out in Applicants' amendment. According to the Examiner the amended claim language is not readily apparent from these sections. The Examiner further states that the specification does not provide a written description or set forth the metes and bounds of this claim language and does not provide direction for the methods encompassing the claim language. According to the Examiner a subgenus is not necessarily described by a genus encompassing it.

Applicants submit that the disclosure specifically recites methods and assays for determining agonist and antagonist activity by for example measuring IL-8 production or NF-κB activation in Examples 1 and 11, in addition to the Examples 14-19. It is understood that the specification is not limited to these two compounds for indicating that the tested material is an agonist or antagonist of the EDG receptor. Specifically, it is also disclosed that GM-CSF is a cytokine, the production of which can be observed. On page 29, lines 6-7 it is disclosed that NF-κB activation results in the production of the cytokines IL-8, IL-6 and GM-CSF. Applicants have amended claim 58 by replacing the term "MCP" for the correct term "GM-CSF". Furthermore, with respect to GTPγS applicants submit that it is generally known in the field of

signal transduction that activation through G-protein coupled receptors requires signaling through G-proteins. Further it is known that G-protein signaling of such receptors requires GTP binding. Therefore, disclosing that the EDG is such a G-protein coupled receptor provides sufficient support for those of skill in the art to understand that measuring GTPγS binding indicates whether the tested material is an agonist or antagonist of the receptor using the assays as described in the disclosure.

Therefore, Applicants submit that claims 55 and 58 are supported by the disclosure in the specification as under 35 U.S.C 112, first paragraph. Accordingly, withdrawal of the rejection is respectfully requested.

The Examiner also rejected claims 44-51 under 35 USC § 112, first paragraph, for lack of enablement in the specification for a method of identifying a compound as an agonist for an EDG receptor or a method of identifying a compound as an antagonist for an EDG receptor using the readouts of NF-κB activation and/or IL-8 production. According to the Examiner the claims are not supported by an enabling disclosure because the specification teaches IL-8 production only in the presence of activated EDG-4 receptor and the NF-κB is taught not to be induced in the presence of activated EDG-1 receptor. Thus, according to the Examiner the recited assays cannot be used to determine agonist/antagonist activity for all types of EDG receptors. Further a large quantity of experimentation is necessary according to the Examiner to identify a compound as an agonist or an antagonist for all EDG receptors. Therefore, the Examiner asserts that undue experimentation is required to make or use the claimed invention in its full scope.

Applicants submit that the disclosure is enabling for determining whether a compound is an agonist or antagonist for an EDG receptor of known activation of NF-κB and production of

cytokines such as IL-8. The Examiner rejects these claims asserting that not all EDG receptors activate NF-κB and therefore the assay in not enabled for those receptors. However, claims 44-51 as amended, are directed to a method of determining whether a compound is an agonist or antagonist for an EDG receptor which activate NF-κB and/or produce IL-8. Further, the disclosure specifically recites methods and assays for determining agonist and antagonist activity by for example measuring IL-8 production or NF-κB activation in Examples 1 and 11, in addition to the Examples 14-19.

Therefore Applicants submit that claims 44-51 are enabled under 35 U.S.C. § 112, first paragraph. Accordingly, withdrawal of the rejection is respectfully requested.

The Examiner also rejected claims 52-59 under 35 USC §112, first paragraph, for failing to comply with the enablement requirement. According to the Examiner the claims are drawn to a method of identifying a compound as an agonist or antagonist of an EDG receptor as identified by the amino acid sequence selected from the group consisting of the amino acid sequence comprising SEQ ID No:2 and SEQ ID No:4, comprising the steps of culturing the cells which express an EDG receptor; contacting said cultured cells with a compound to be tested for agonist or antagonist activity and measuring an appropriate response. The Examiner asserts that SEQ ID No:2 and SEQ ID No:4 are nucleic acid sequences and not amino acid sequences and that there is no disclosure in the application on how to make the amino acid sequences from the nucleic acid sequences. In addition, the Examiner asserts that the specification fails to teach how to identify a compound as an agonist or antagonist of an EDG receptor wherein the activity is measured by modulation of cellular cyclic AMP levels and GTPγS binding. According to the Examiner the specification fails to disclose a protocol and the proper parameters/controls when employing

these experiments.

Applicants have incorporated claim 52 in claims 53 and 54 and replaced the sequence identifiers SEQ ID No:2 and SEQ ID No:4 with the correct SEQ ID No:17 and SEQ ID No:22 respectively. The sequences identified in claims 53 and 54 as amended are amino acid sequences for which the specification clearly provides support. Further, with respect to the Examiner's rejection based on measuring the modulation of cellular cyclic AMP levels, applicants direct the Examiner's attention to Example 10A on page 35 where such an assay are specifically disclosed. Moreover, as discussed above, it is generally known in the field of signal transduction that activation through G-protein coupled receptors requires signaling through G-proteins. Further it is known that G-protein signaling of such receptors requires GTP binding. Therefore, disclosing that the EDG is such a G-protein coupled receptor provides sufficient support for those of skill in the art to understand that measuring GTPγS binding indicates whether the tested material is an agonist or antagonist of the receptor using the assays as described in the disclosure.

Therefore, Applicants submit claims 53-59 (claim 52 being cancelled) are enabled by the disclosure in the specification as under 35 USC §112, first paragraph. Accordingly, withdrawal of the rejection is respectfully requested.

The Examiner also rejected claims 44-59 under 35 USC §112, second paragraph, as being indefinite. According to the Examiner claims 44-51 are indefinite because the recitation, "measuring a response indicative of the degree of NF-κB activation" and "measuring a response indicative of the degree of IL-8 production". The Examiner asserts that the responses are the same for identifying a compound as an agonist and identifying a compound as an antagonist, and thus it is unclear to discern the difference between agonist and antagonist. Further the Examiner

states that "indicative of the degree of activation" and "indicative of the degree of production" is vague because the metes and bounds of the claims cannot be determined. In addition, the Examiner suggests that applicants amend the claims to recite "lysolipid" instead of "LL". Further, according to the Examiner claims 52-59 are indefinite because of the recitation, "measuring an appropriate response indicative of the degree of agonist or antagonist activity". The Examiner asserts that the claims fail to teach how to discern agonist and/or antagonist activity. The Examiner further asserts that claims 55 and 57 are indefinite because it is unclear whether the terms "modulation" and "determining the level" mean an increase or decrease. In addition, according to the Examiner claim 52 is indefinite because SEQ ID No:2 and SEQ ID No:4 are polynucleotides, not amino acid sequences as recited in the claim. Also, the Examiner asserts that in claim 52 there are two different identifiers (a) and (b) recited. Further, the Examiner asserts that claim 55 recites an improper Markush group. Claim 58 was indefinite because according to the Examiner IL-8 and IL-6 are misspelled.

Applicants submit that claims 44-51, as amended, clearly define the subject matter of the invention because the claim language "measuring a response indicative of the degree of NF-κB activation" and "measuring a response indicative of the degree of IL-8 production" is adequately described in the disclosure. The disclosed measured responses for both NF-κB activation and IL-8 production are indirect measurements, for example using a reporter gene construct (NF-κB) or an ELISA (IL-8). Further it is disclosed that these measured responses are time and dose dependent. Therefore, the measured response is indicative of NF-κB activation and IL-8 production respectively. Furthermore, the degree of response reflects the degree of NF-κB activation and IL-8 production respectively both qualitatively and quantitatively. Therefore, in

light of the disclosure one skilled in the art would clearly understand the particulars of the claimed methods in determining whether tested material is an agonist or antagonist for the EDG receptor. However, to more clearly claim the subject matter of the invention. Applicants amended claims 44, 46, 48 and 50 to recite step (c) as "identifying a compound as an agonist/antagonist by quantitatively determining NF-κB activation/IL-8 production in said cultured cells." Applicants also amended claims 48 and 50 to more clearly describe the claimed invention by replacing the "LL" with the term "lysolipid". Further, with respect to the indefinite rejections of claims 52-59, applicants have cancelled claim 52 and incorporate the language of claim 52 into both claims 53 and 54 while also replacing SEQ ID NO:2 and 4 with the correct SEQ ID NO:17 and 22 of the amino acid sequences as recited and correcting one set of (a) and (b) identifiers to (i) and (ii). Thus, applicants submit it is clear that claim 53, as amended, is directed to measuring an agonist response and claim 54 to measuring an antagonist response. Further, this amendment also makes the rejections with respect to whether an increase or a decrease is measured in claim 55 and 57 moot, as agonist activity results in an increase in receptor response whereas antagonist activity (in claims 54 and 60-64) results in a decrease or inhibition of receptor response.

Therefore, applicants submit that claims 44-59, as amended, more clearly define the subject matter of the invention as under 35 USC §112, second paragraph. Accordingly, withdrawal of the rejection is respectfully requested.

The Examiner further rejected claims 44-51 in the pending application under 35 USC §102 (b) as anticipated by Hecht et al (The Journal of Cell Biology, Vol.135/4, November, 1996). According to the Examiner, Hecht et al teach that LPA is the endogenous ligand for EDG-2

receptor and that other phospholipids did not produce the same effect as LPA. The Examiner asserts that the claims are drawn to methods of identifying compounds as an agonist or antagonist for an EDG receptor comprising measuring a response indicative of the degree of NF-κB activation and indicative of the degree of IL-8 production. According to the Examiner the claims do not have a precise step of actually measuring something that is indicative of NF-κB activation and/or IL-8 production. The Examiner suggests that applicants amend the claims to recite measuring NF-κB activation or measuring IL-8 production.

Applicant submit that claims 44-51 as amended are not anticipated by Hecht et al. Claims 44-51, as amended, are directed to in step (c) "identifying a compound as a agonist/antagonist by quantitatively determining NF-κB activation/IL-8 production in said cultured cells." Thus, claims 44-51 positively recite measuring NF-κB activation or measuring IL-8 production as a method for identifying a compound as a agonist/antagonist for an EDG receptor, a method not disclosed in Hecht et al. Applicants further point out that the activity observed in Hecht et al is not quantitative and therefore also does not anticipate the claimed invention.

Therefore, Applicants submit that claims 44-51 are not anticipated by Hecht et al. Accordingly, withdrawal of the rejection is respectfully requested.

Applicants submit that the present application is now in condition for allowance.

Reconsideration and favorable action are earnestly requested.

RESPECTFULLY SUBMITTED,					
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